The amendments to claims 1-9, as described above, have been made for clarity and/or to correct typographical and grammatical errors. These amendments do not add new matter as described above. New claims 10-27 do not add new matter. Support in the specification and claims, as originally filed, for new claims 10-27 has been detailed above. Accordingly, entry of the amendments to claims 1-9, and new claims 10-27 is respectfully requested.

RESPONSE TO THE RESTRICTION REQUIREMENT

Claims 1-9 are pending in the application and subject to a restriction requirement under 35 U.S.C. § 121 as stated in numbered paragraphs I-V on page 2 of the Office Action mailed June 21, 2002. Applicants respectfully traverse the present restriction requirement as improper under US Patent Office practice and procedure for the restriction of a Markush-type claim. Applicants request reconsideration and withdrawal of the restriction requirement based on the following remarks.

If, notwithstanding Applicants' present request for reconsideration, the Examiner maintains that an Election/Restriction Requirement of some nature should be made, Applicants propose that the claims be divided into alternate restriction Groups A-D, as detailed below.

A. Restriction Is Improper Because There is Unity Of Invention.

In the present Office Action, the Examiner has identified five groups of compounds that restrict Applicants' invention, as provided in numbered paragraphs I-V thereof (Office Action, page 2). The Office requires restriction on the basis that the inventions are "distinct" and that the inventions "have acquired separate status in the art as shown by their different classification" (Office Action, page 3, lines 18-19). In support of the restriction requirement, the Office asserts that

> [S]eparate searches in the literature as well as in the U.S. Patent Classification System would be required. Each group's compounds are made and used independently of each other and

> could support separate patents. The compounds differ significantly in chemical structures. One skilled in the art would not consider such diverse structure equivalents of each other.

Office Action, page 3, lines 7-10.

Under MPEP § 803.02, restriction of a Markush-type claim is improper, even where the claims are directed to what would otherwise be considered independent and distinct inventions, if the subject matter of the claim has unity of invention. As stated in MPEP § 803.02, "unity of invention exists where compounds included within a Markush Group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility."

Applying the standard set forth in the US Patent Office guidelines for the examination of Markush claims, the present restriction requirement is improper because the compounds of the present invention do in fact have clear unity of invention. In particular, the compounds: (1) share a common utility (*i.e.*, they are LFA-1 antagonists); and (2) share a structural feature essential to the common utility, (*i.e.*, they are all phenyl sulfide heterocyclyl "amino" (e.g., $NR^{10}R^{11}$) compounds and the linking sulfide and "amino" are required for utility).

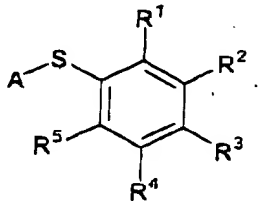
1. Applicants' Compounds Have A Common Utility

Applicants' claimed compounds have a common utility (*e.g.*, they are LFA-1 antagonists). The specification asserts that these compounds bind to the I-domain of LFA-1 and block the interaction of LFA-1 to ICAMs. Applicants' compounds are useful for the treatment of diseases such as inflammatory diseases, autoimmune diseases, tumor metastasis, allograft rejection, and reperfusion injury. Specification, page 4, lines 1-6. The utility Applicants' compounds is demonstrated by the *in vitro* testing described in Examples 97A and 97B of the specification on pages 113-116. Specifically, the compounds of the invention "inhibit the binding of ICAM-1 to LFA-1 with an IC_{50} of less than 20 micromolar." (Specification, page 115, lines 3-4.)

2. Applicants' Compounds Have Common Structural Features Essential to the Asserted Utility.

Applicants' claimed compounds share a structural feature essential to the common utility, (*i.e.*, they are all phenyl sulfide heterocycle "amino" compounds and the linking sulfide and amine are required for utility). Under, *In re Harnich*, claimed compounds are part of a single invention and a Markush grouping is proper where there is "a single structural similarity," and the "claimed compounds all belong to a subgenus . . . which is not repugnant to principles of scientific classification." *In re Harnich*, 206 USPQ 300, 631 F.2d 716, 721 (CCPA 1980), submitted herewith.

Formula I, representing Applicants' claimed compound genus, is shown below.



Formula I

Formula I above shows that each compound within Applicants' claimed compound genus has a common phenyl sulfide structure. Further, Applicants claimed compounds each have an "amino" moiety, *e.g.*, an $NR^{10}R^{11}$ group, as shown in Formula II (*see*, e.g., Specification, page 4, line 14). Thus, Applicants' invention comprises not only a "single structural similarity," as required under *In re Harnisch*, but two. Accordingly, the compounds within Applicants' invention can be appropriately classified and searched together.

Further, it is Applicants' position that the common phenyl sulfide structure, and "amino" moiety, are essential to the asserted utility of the compounds. The present invention discloses a series of aryl phenyl sulfide "heterocyclyl" amino compounds. In the *Expert Opin. Ther. Patents* article to Liu, G. (submitted to the US PTO in the Supplemental Information

Disclosure Statement and accompanying PTO Form 1449, dated April 2, 2002), a number of diaryl sulfide species, including an earlier discovered diaryl sulfide anilino compound, are identified. *See*, Liu, G., *Expert Opin. Ther. Patents* (2001) 11(9):1387. This article specifies that both the sulfide and the anilino group are required for the affinity that results in the utility of the compounds as LFA-1 antagonists.

Although examination of Applicants' claimed invention may involve searching in multiple subclasses, this is not the test for an appropriate restriction requirement for Markush-type claims. Provided that the Markush group has "common utility" and a "common structural feature," essential to that utility, as is the case here, the Markush group is proper under the Patent Office guidelines. MPEP § 803.02. Accordingly, Applicants respectfully request reconsideration and withdrawal of the Restriction/Election requirement.

B. The Restriction Requirement Is Improper For Groups That Are Classifiable Together.

In the present Office Action, Applicants' invention is restricted into Groups III and IV, which are both classified in class 548. Restriction of an invention that is classified together is improper, unless the Office provides evidence of separate status in the art, and also a separate field of search. Where the classification is the same and the field of search is the same and there is no clear indication of separate future classification and field of search, no reasons exist for dividing among related inventions. MPEP § 808.02.

In the present case, the Office has not provided any evidence of separate status in the art for Groups III and IV, and has not indicated that a different field of search is required. In support of the restriction requirement, the Office states that "each group's compounds are made and used independently of each other and could support separate patents. The compounds differ significantly in chemical structures. One skilled in the art would not consider such diverse structure equivalent of each other."

In response, Applicants would like to point out that Groups III and IV both contain 5-membered heterocycles containing 1 N atom and another heteroatom, either O or S

(representing oxazoles and thiazoles, respectively). Further, Scheme 1 and Scheme 3 in the specification, pages 29-30, clearly shows that the compounds within Groups III and IV can be formed from the same intermediate compound (*i.e.*, compound 3), in similar synthetic procedures, which employ different reagents, to arrive at either the desired oxazole compounds (*e.g.*, compound 4), or thiazole compounds (*e.g.*, compound 10).

The Office also states that the "inventions are distinct for the reasons given above and have acquired separate status in the art as shown by their different classification." Office Action, page 3. This assertion is clearly without basis as applied to Groups III and IV, as these Groups have the same classification, *i.e.*, Class 548.

Thus, given that the compounds within Groups III and IV have the same classification within the U.S. Patent Classification System, similar chemical structures, and similar synthetic preparations, the Office has clearly not met the burden of showing evidence of separate status, or a separate field of search, as required for proper restriction. Applicants request withdrawal of the restriction requirement on this basis.

C. Proposed Election/Restriction Requirement

If, notwithstanding Applicants' present request for reconsideration, the Examiner maintains that an Election/Restriction Requirement of some nature should be made, Applicants propose that the claims be divided into the following Groups A-D.

A. Claims 1-14, and 16-27 (in part), drawn to compounds, compositions, methods of use, and processes of making compounds, where R^1 or R^3 is a 6- membered heterocycle containing 2 N atoms, classified in class 544.

B. Claims 1-14, and 16-27 (in part), drawn to compounds, compositions, methods of use, and processes of making compounds, where R^1 or R^3 is a 6- membered heterocycle containing 1 N atom, classified in class 546, subclass various.

C. Claims 1-15, and 17-27 (in part), drawn to compounds, compositions, methods of use, and processes of making compounds, where R^1 or R^3 is a 5- membered

heterocycle containing 1 N atom and another heteroatom, classified in class 548, subclass various.

D. Claims 1-27 (in part), drawn to others, classified in various classes and subclass various.

Although Applicants do not agree with the propriety of an Election/Restriction requirement at this time, to advance prosecution of this case, alternate Groups A-D are proposed above. In view of the common structural features and common utility of the compounds of the present invention, as discussed above, and the common classification, the Examiner is urged to accept the above-proposed restriction/election. If the above-proposed restriction/election is not at this time acceptable to the Examiner, the Applicants respectfully request further discussion regarding the restriction of the invention under 35 U.S.C. §121.

D. Provisional Election.

If, notwithstanding Applicants' present request for reconsideration, the Examiner maintains that an Election/Restriction Requirement of some nature should be made, and the Examiner accepts the alternate Election/Restriction Groups A-D above, Applicants provisionally elect, with traverse, Group A. Claims 1-14, and 16-27 are readable on Group A.

If, notwithstanding Applicants' present request for reconsideration, the Examiner maintains that an Election/Restriction Requirement of some nature should be made, and the Examiner does not accept the alternate Election/Restriction Groups A-D above, Applicants provisionally elect, with traverse, Group I. Claims 1-14, and 16-27 are readable on Group I.

CORRESPONDENCE ADDRESS.

Initially, it is noted that the Office Action mailed June 21, 2002 was sent to the law firm of Marshall Gerstein & Borun. The undersigned attorney requests that the Examiner address all communications to Jeffrey G. Sheldon, Esq., of Sheldon & Mak, 225 South Lake